SUBCOMMITTEE ON PUBLIC BUILDINGS AND GROUNDS

REGARDING H.R. 881: A BILL TO PROHIBIT SMOKING IN FEDERAL BUILDINGS

COMMENTS OF MAURICE LEVOIS, PH.D.
APRIL 16, 1993

In addition to my oral comments and the written comments that accompanied my appearance before this subcommittee, I should note that I have also submitted written answers to specific written questions posed by Congressman Emerson. Those questions had to do with what I regard as EPA's inappropriate use of tests of statistical significance. This topic is closely tied to other problems I see in the EPA's selective use of the available data. I would like to take this opportunity to point out some of the other problems.

Spousal smoking is a biased definition of ETS exposure.

A fundamental problem with the ETS epidemiologic study design is that all of the studies use spousal smoking as the basic definition of ETS exposure. Spousal smoking is not just an imprecise definition (i.e. resulting in nondifferential misclassification of exposure). It is also biased.

It is generally recognized that the spousal smoking definition leads to selective misclassification of active smokers. Since spouses of smokers in ETS studies are more likely to be current or former smokers themselves, the spousal smoking study design produces a biased estimate of the association of lung cancer and ETS exposure. Attempts at *post hoc* correction for possible effects of smoker misclassification, such as employed by the EPA in their

ETS risk assessment, are not based upon sound data. The assumptions employed in such exercises simply reflect the biases of the authors. *Post hoc* correction cannot be regarded as an acceptable substitute for employing an unbiased study design.

In addition, the spousal smoking definition of ETS exposure confounds many lung cancer risk factors (such as socioeconomic status, prior lung disease, diet, and occupational exposure) that are shared by spouses and are known to be more common in households where there is a smoker.

Biases introduced when spousal smoking is employed as a proxy for ETS exposure could easily be responsible for the very weak pooled spousal smoking / lung cancer association reported in a number of studies. It is noteworthy that meta-analysis of results of studies that have looked at ETS exposure in the workplace (as opposed to using spousal smoking as the ETS exposure definition) shows no increase in ETS related lung cancer risk. This important discrepancy undermines both the validity of the spousal smoking proxy and the inference that ETS exposure causes lung cancer.

Meta-analysis compounds bias in ETS epidemiologic data.

Meta-analysis (or pooling) of ETS epidemiologic data cannot correct for biases introduced by the spousal smoking definition of ETS exposure. However, meta-analysis can make the effects of biases introduced by the spousal smoking study design appear statistically significant. Because the individual ETS studies are flawed, meta-analysis of these studies is not a valid approach to

ETS risk assessment. Despite this objection, EPA has relied exclusively on meta-analysis of spousal smoking epidemiologic data, and numerous related assumptions, to arrive at their ETS / lung cancer risk estimate. For this reason it is necessary to examine critically the EPA's meta-analysis methodology.

There are instances in which EPA has selected as the best summary risk estimate for a published ETS research report a value that is at odds with the stated conclusions of the authors of the report. This sort of selective use of the data is unavoidable whenever a meta-analysis is performed. It is essential that a meta-analysis be conducted according to a clear and specific set of rules for selecting one result that best represents each study. Since most ETS epidemiologic studies employ numerous operational definitions to characterize study factors, and report numerous results, if there were no prior rule for selection, then a statistician could easily bias the meta-analysis through biased selection of results.

The risk of lung cancer mortality in wives of smokers compared to the risk in wives of nonsmokers defines the overall spousal exposure relative risk for each study. This is the result traditionally used to represent each study in an ETS meta-analysis because it is the most uniform result across all of the studies, and it takes advantage of the most data. This value may not always be reported, but in almost every case it can be calculated based upon other data published in the reports. If an overall spousal smoking relative risk is not stated, and it cannot be calculated,

then the study cannot be used in an ETS meta-analysis, regardless of the claims made by the authors.

Multiple comparison bias.

Because both ETS exposure and lung cancer are often defined in a variety of ways in a single study there is often a question as to the meaning of inconsistent or contradictory results. For example, in a single study the researchers may define 'ETS exposure' as: ever- versus never- exposed to ETS as a child, as a spouse, or in the workplace; as years of childhood, spousal, or workplace ETS exposure; as the average number of packs of cigarettes smoked by parents, spouse, or co-workers; as 'pack X years' of exposure as a child, spouse, or in the workplace. The researchers will then proceed to run numerous analyses on a combination of these and other definitions derived from looking at multiple lung cancer cell types and/or other subsets of the cases and controls.

When many closely related significance tests are conducted in a single study, and the results of only one or two of the tests are reported, the nominal significance levels of the results are not valid. In reporting the results of ETS epidemiologic studies the authors are usually able to select from among multiple results, and generally ignore the fact that multiple comparisons may have biased the nominal significance levels that are reported.

Epidemiologic research reports must be read critically. Such observational studies are not entirely objective. Reporting biases are a consequence of the common practice of employing multiple

operational definitions of study factors. A critical reader should evaluate the adequacy of a study's design, the way in which cases and controls are selected, the way in which exposures and outcomes are defined, the attention paid to potential sources of artifact, and the completeness of the final study report. The ETS epidemiologic studies do not stand up well to such critical evaluation.

One-sided versus two-sided significance tests.

Given the serious flaws in the underlying spousal smoking study design, the strong conclusions often stated by authors of these studies are not convincing. Debating the statistical significance of reported ETS results may only serve to distract attention from the fact that the results are biased in the first place. However, keeping fundamental study adequacy issues in mind, it is important to evaluate the EPA's use, or misuse, of statistical significance tests to support their conclusions.

The first draft of the EPA's ETS risk assessment used a standard two-sided, 95% significance test for the main spousal smoking analysis. In their final risk assessment, after seeing the data and noting that the standard test would not have been statistically significant, the EPA shifted to a one-sided, 90% significance test. This is a biased statistical approach that is contrary to accepted standards (Armitage and Berry, 1987; Fleiss, 1973).

Prior to release of the final EPA risk assessment new spousal

smoking data were published that brought the pooled lung cancer risk estimate down to a level that is not even significant using a one-sided 90% confidence level. Such statistical instability plainly contradicts EPA's claim of "medium to high" confidence in their ETS risk estimate, and underscores the need for higher scientific standards than have been employed in the ETS risk assessment.

Conclusion.

There are fundamental flaws in the EPA's ETS risk assessment. The ETS epidemiologic data are derived from a flawed spousal smoking study design. Meta-analysis of biased spousal smoking study data compounds the effects of bias, and is not a valid methodology for ETS risk assessment. Recent contradictory study results have been ignored by EPA, as have the contradictory data from studies of ETS exposure in the workplace which do not show a risk elevation. The use of one-sided, 90% significance tests, after viewing the data and observing that use of the standard two-sided, 95% confidence level would not produce a significant result, is contrary to accepted statistical methodology and reflects a clear bias in favor of statistical significance at the expense of stability and confidence. The EPA's ETS risk assessment should not be relied upon as an unbiased estimate of the purported risk of ETS exposure because it exploits flawed data and employs biased, unscientific methods.

2023468363